Sub A1

23. An aerosol composition comprising:

(a) aggregates of a freeze-dried powder comprising nanoparticulate drug particles, wherein the aggregates of freeze-dried drug are less than or equal to about 100 microns in diameter and the nanoparticulate drug particles:

C2

(i) comprise a poorly soluble crystalline drug, wherein by "poorly soluble" it is meant that the drug has a solubility in at least one liquid dispersion medium of less than about 10 mg/ml,

(ii) have an effective average particle size of less than about 1000 nm, meaning at least 50% of the drug particles have a particle size of less than about 1000 nm, and

(iii) have a surface modifier adsorbed on the surface thereof,

wherein the freeze-dried powder aggregates are formulated into an aerosol composition.

Sub A1

35. An aerosol composition for use in a propellant-based pMDI comprising:

(a) dry powder aggregates of a nanoparticulate poorly-soluble crystalline drug, wherein by "poorly soluble" it is meant that the drug has a solubility in at least one liquid dispersion medium of less than about 10 mg/ml, wherein the aggregates are less than or equal to about 100 microns in diameter, and wherein the drug:

C3

(i) has a surface modifier adsorbed on the surface thereof, and

(ii) has an effective average particle size of less than about 1000 nm, meaning at least 50% of the drug particles have a particle size of less than about 1000 nm, and

(b) a non-aqueous propellant,

wherein the dry powder aggregates and non-aqueous propellant are formulated into a dry powder aerosol for use in a propellant-based pMDI.

40. A method of making an aerosol composition comprising:

(a) forming an aqueous nanoparticulate dispersion of a poorly soluble drug, wherein:

(i) the dispersion comprises poorly soluble crystalline drug particles and a surface modifier adsorbed on the surface thereof, wherein by "poorly soluble" it is meant that the drug has a solubility in the liquid dispersion medium of less than about 10 mg/ml, and

(ii) the drug particles have an effective average particle size of less than about 1000 nm, meaning at least 50% of the drug particles have a particle size of less than about 1000 nm;

(b) spray-drying the nanoparticulate dispersion to form a dry powder of aggregates of the nanoparticulate drug and surface modifier particles, wherein the aggregates have a diameter of less than or equal to about 100 microns; and

(c) formulating the dry powder aggregates into an aerosol composition.

42. A method of making an aerosol composition comprising:

(a) milling under non-pressurized conditions in a non-aqueous medium having a high boiling point the following:

(i) a poorly soluble crystalline drug, wherein by "poorly soluble" it is meant that the drug has a solubility in the non-aqueous medium of less than about 10 mg/ml, and

(ii) a surface modifier, to obtain a nanoparticulate drug composition having an effective average particle size of less than about 1000 nm, meaning at least 50% of the drug particles have a particle size of less than about 1000 nm,

(b) evaporating the non-aqueous medium to obtain a dry powder of aggregates of drug and surface modifier particles, wherein the aggregates have a diameter of less than or equal to about 100 microns; and

(c) formulating the dry powder aggregates into an aerosol composition.

43. A method of making an aerosol composition comprising:

(a) milling under pressurized conditions in a non-aqueous medium the following:

(i) a poorly soluble crystalline drug, wherein by "poorly soluble" it is meant that the drug has a solubility in the non-aqueous dispersion medium of less than about 10 mg/ml, and

(ii) a surface modifier, to obtain a drug having an effective average particle size of less than about 1000 nm, meaning at least 50% of the drug particles have a particle size of less than about 1000 nm;

(b) evaporating the non-aqueous medium to obtain a dry powder of aggregates of drug and surface modifier particles, wherein the aggregates have a diameter of less than or equal to about 100 microns; and

(c) formulating the dry powder aggregates into an aerosol composition.

44. A method of making an aerosol composition comprising:

(a) forming an aqueous nanoparticulate dispersion of a poorly soluble drug, wherein:

(i) the dispersion comprises poorly soluble crystalline drug particles, wherein by "poorly soluble" it is meant that the drug has a solubility in the liquid dispersion medium of less than about 10 mg/ml, and wherein the drug particles have an effective average particle size of less than about 1000 nm, meaning at least 50% of the drug particles have a particle size of less than about 1000 nm, and

(ii) a surface modifier adsorbed on the surface thereof;

(b) freeze-drying the nanoparticulate dispersion to form a dry powder of aggregates of the nanoparticulate drug and surface modifier particles, wherein the aggregates have a diameter of less than or equal to about 100 microns; and

(c) formulating the freeze-dried powder aggregates into an aerosol composition.

65. The method of claim 42, wherein at least 70% of the drug particles have a particle size of less than about 1000 nm.

66. The method of claim 42, wherein at least 90% of the drug particles have a particle size of less than about 1000 nm.

67. The method of claim 43, wherein at least 70% of the drug particles have a particle size of less than about 1000 nm.

68. The method of claim 43, wherein at least 90% of the drug particles have a particle size of less than about 1000 nm.

69. The method of claim 44, wherein at least 70% of the drug particles have a particle size of less than about 1000 nm.

70. The method of claim 44, wherein at least 90% of the drug particles have a particle size of less than about 1000 nm.

REMARKS

Applicants respectfully request reconsideration of this application.

I. Summary of the Claims

Following entry of this amendment, claims 11-36, 40-45, 47-49, and 51-117 are pending. Claims 11, 23, 35, 40, 42, 43, and 44 were amended to incorporate the limitations in the preamble of the claims into the body of the claims. In addition, claims 65-70 were amended to recite "a method" rather than "an aerosol composition," to correct a lack of antecedent basis for the original claim language.

The foregoing amendments do not introduce new matter. It is acknowledged that these amendments are submitted after final rejection of the application. However, because the amendments place the application in condition for allowance, or at least in better condition for appeal, entry thereof by the Examiner is respectfully requested.